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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,544	03/01/2004	Miroslav Colic	4904-4DIV	9685

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EXAMINER
XIE, XIAOZHEN

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,544	COLIC, MIROSLAV	
	Examiner	Art Unit	
	XIAOZHEN XIE	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 17-23* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,19 and 21-23* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20080221*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

The Information Disclosure Statement (IDS) filed 21 February 2008 has been entered. Applicant's amendments of the specification and the claims received on 21 February 2008 have been entered.

Claims 1-14 and 16 have been cancelled. Claims 15 and 17-23 are pending. Claim 20 is withdrawn from further consideration as being drawn to a nonelected species. Claims 15, 17-19 and 21-23 are under examination to the extent they read on the elected species (i.e., the pharmaceutical composition further comprises pro-oxidant metal complexes and a cytokine which is IL-12).

Specification

The objection to the specification for failing to update the status of the related applications is withdrawn in response to Applicant's amendment of the specification.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The amended claims 15, 17, 19 and 21-23 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method of treating a tumor in a patient afflicted with the disease comprising administering to the patient a pharmaceutical composition comprising a zeolite, wherein the zeolite is clinoptilolite that has a mean particle size of 250 nm,* does not reasonably provide enablement for administering zeolite of any sizes. The basis of this rejection is set forth in the previous office actions.

Applicant argues that the claims as amended now recite a therapeutic method using zeolites having an average particle size of about 6 microns or less. Applicant argues that the specification teaches the preferred size range recited in the amended claims, e.g., "preferred average particle size is about 6 microns or less, preferably about 0.5 to 5 microns, and more preferably about 1.5 microns", and the only mention of sedimentation is as a technique which can be used to remove particles larger than 5 microns. Applicant argues that the adverse zeolite properties taught by the Pavelic article relate only to "large" micro sized particles, rather than the smaller sized particles used in the invention as claimed. Applicant cites Pavelic et al. and argues that the zeolites ("MZ") used by Pavelic et al. to treat tumors in dogs had a broad size range (pp. 712, Figure 1C, and col. 2), falling almost entirely within that recited in the amended claims. Applicant argues that such particle sizes which behaved successfully in therapy

fall within the claim limit of about 6 microns or less and well above the 0.25 μm size which the Examiner asserts is the only size enabled.

Applicants' argument has been fully considered but has not been found to be persuasive.

Applicant's amendment of the claims is not sufficient to overcome the rejection even in view of the Pavelic et al. reference, because the instant invention requires the pharmaceutical composition comprising a zeolite to be injected into the patient. In the Pavelic et al. reference, the mechanically treated natural clinoptilolite (MZ), which falls almost entirely within that recited in the amended claims, was administered orally either through gavage or supplemented as powder to the conventional food (mice, rats), or in capsules (dogs) which were again admixed to food. Pavelic et al. specifically teach that this is because of the insolubility of the tested substance (pp. 710, col. 2, last paragraph bridging pp. 711, col. 1).

As stated previously, Applicant has disclosed three different uses of the nano-engineered zeolite: 1) the nano-engineered zeolite can be used to encaptulate metal complexes that act as an antioxidants or prooxidants (catalytic salen-metal antioxidants or prooxidants with cobalt, maneganeses, ion, rhodium and palladium) (Example I). In this case, a mean particle size is about 500 nm (pp. 16, lines 10-17). The disclosure shows in Example IV that the nano-engineered zeolite was administered in the form of a mice chow (orally) to mice of various tumor models (lung, colorectal, and breast adenocarcinoma and melanoma), and exhibited anti-cancer activity in the animals (pp. 32, lines 5-19). 2) Clinoptilolite with a mean particle size of 250 nm can be used as a

vaccine adjuvant to enhance the immunogeneity of proteins, cell parts or whole cell vaccines. In such case, the clinoptilolite was injected near the tumor site to attract lymphocytes, and significant infiltration of lymphocytes and tumor remission were observed with melanoma, adenocarcinomas of lung and colorectal models (Example VII); and 3) The specification also teaches that the zeolite can be used to incorporate small drugs, macromolecules or whole cells for a delayed sustained release. Therefore, Applicant has not provided sufficient guidance and support for administering (e.g., by injecting) a zeolite having a particle size range as recited in the claims. Further, the claims 19 and 21 recite "wherein the pharmaceutical composition further comprises at least one of a pro-oxidant metal complex and a cytokine which is IL-12". The specification does not provide support how to maintain IL-12 activity if it is administered into a patient other than by injection, e.g., by orally. As for Applicant's argument that the adverse zeolite properties taught by the Pavelic article relate only to "large" micro sized particles, rather than the smaller sized particles used in the invention as claimed, Brown et al. (EP0384070) teaches the use of zeolite P in detergent compositions, wherein the particle sizes are in the range from 0.1 to 5.0 microns, falling within the scope of the recited range. Thus, the scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification. The artisan would not know how to practice the invention as broadly claimed without undue experimentation.

Allowable Subject Matter

Claim 18 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

NO CLAIM IS ALLOWED.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
May 6, 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646